Claims

1. A method to monitor the expression of a gene, which method comprises:

a) delivering to a multi-cellular organism a nucleic acid encoding a fluorophore operatively linked to the promoter of a gene whose expression is to be analyzed or delivering a cell containing said nucleic acid; and

b) observing the presence, absence or intensity of the fluorescence generated by said fluorophore at various locations in said organism by whole-body external fluorescent optical imaging, whereby the expression of said gene is monitored.

2. The method of claim 1, wherein a nucleic acid encoding a fluorophore operatively linked to the promoter of the gene is delivered to the organism.

3. The method of claim 1, wherein the nucleic acid is comprised in a viral vector.

4. The method of claim 3, wherein the viral vector is derived from adenovirus.

5. The method of claim 1, wherein a cell containing the nucleic acid is delivered to the organism.

6. The method of claim 5, wherein the cell is delivered to the organism via a surgical procedure.

7. The method of claim 6, wherein the cell is delivered to the organism via direct implantation by surgical orthotopic implantation (SOI) at a desired site.

8. The method of claim 1, wherein the fluorophore is a humanized fluorophore.

9. The method of claim 1, wherein the fluorophore is selected from the group consisting of a green fluorescent protein (GFP), a blue fluorescent protein (BFP) and a red fluorescent protein (RFP).

10. The method of claim 9, wherein the GFP is the humanized hGFP-S65T.

11. The method of claim 1, wherein the multi-cellular organism is a plant or an animal.

12. The method of claim 11, wherein the animal is a mammal.

13. The method of claim 12, wherein the mammal is selected from the group consisting of a mouse, a rat, a rabbit, a cat, a dog, a pig, a cow, an ox, a sheep, a goat, a horse, a monkey and a non-human primate.

14. The method of claim 11, wherein the animal is a transgenic animal.

15. The method of claim 1, wherein the gene is expressed in a tissue or organ specific manner.

16. The method of claim 15, wherein the tissue is selected from the group consisting of connective, epithelium, muscle and nerve tissues.

17. The method of claim 15, wherein the organ is selected from the group consisting of brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, gland, and internal blood vessels.

18. The method of claim 1, wherein the gene is a tumor or cancer associated gene.

19. The method of claim 18, wherein the tumor or cancer associated gene is an oncogene or a tumor suppressor gene.

20. A method to evaluate a candidate protocol or drug for treating a disease or disorder, which method comprises:

a) administering said protocol or drug to a non-human mammalian subject which expresses a fluorophore under the direction of a promoter of a gene associated with said disease or disorder, and determining the expression of said gene via observing the presence, absence or intensity of the fluorescence generated by said fluorophore at various locations in said mammalian subject by whole-body external fluorescent optical imaging;

b) determining the expression of said gene, via observing the presence, absence or intensity of the fluorescence generated by said fluorophore at various locations in said mammalian subject by whole-body external fluorescent optical imaging, in a control non-human mammalian subject which expresses said fluorophore under the direction of said promoter of said gene; and

c) comparing the expression of said promoter determined in steps a) and b), wherein the expression determined in step a) is different from that in step b) identifies said protocol or drug as effective in treating the disease or disorder.

21. The method of claim 20, wherein overexpression of the gene is associated with the disease or disorder and the expression determined in step a) is lower than that in step b) when said protocol or drug is effective in treating the disease or disorder.

22. The method of claim 20, wherein underexpression of the gene is associated with the disease or disorder and the expression determined in step a) is higher than that in step b) when said protocol or drug is effective in treating the infection.

23. The method of claim 20, wherein the disease or disorder is selected from the group consisting of a cancer, an immune system disease or disorder, a metabolism disease or disorder, a muscle and bone disease or disorder, a nervous system disease or disorder, a signal disease or disorder and a transporter disease or disorder.

24. The method of claim 20, wherein the promoter is derived from an infectious organism.

25. The method of claim 20, wherein the non-human mammalian subject which expresses a fluorophore under the direction of a promoter of the gene is produced by delivering a nucleic acid encoding the fluorophore operatively linked to the promoter of the gene, or delivering a cell containing the nucleic acid, to the non-human mammalian subject.

26. The method of claim 20, wherein the non-human mammalian subject is selected from the group consisting of a mouse, a rat, a rabbit, a cat, a dog, a pig, a cow, an ox, a sheep, a goat, a horse, a monkey and a non-human primate.

27. The method of claim 24, wherein the non-human mammalian subject is an infectious disease animal model.

28. The method of claim 20, wherein the non-human mammalian subject is a transgenic animal.

29. The method of claim 20, wherein the fluorophore is selected from the group consisting of a green fluorescent protein (GFP), a blue fluorescent protein (BFP) and a red fluorescent protein (RFP).

30. The method of claim 24, wherein the infectious organism is selected from the group consisting of a fungus, a bacterium and a virus.

31. The method of claim 30, wherein the fungus is a yeast.

32. The method of claim 30, wherein the bacterium is an eubacteria or an archaebacteria.

33. The method of claim 30, wherein the virus is selected from the group consisting of a Class I virus, a Class II virus, a Class III virus, a Class IV virus, a Class V virus and a Class VI virus.

34. The method of claim 24, wherein the candidate drug to be screened is an antibiotic.

35. The method of claim 1, wherein the expression of more than one gene is monitored simultaneously.

36. The method of claim 20, wherein more than one candidate protocol or candidate drug is screened for simultaneously.

37. A method to screen for a modulator of the expression of a gene in a multi-cellular organism, which method comprises:

a) administering a test substance to a non-human multi-cellular organism which expresses a fluorophore under the direction of a promoter of a gene, and determining the expression of said promoter via observing the presence, absence or intensity of the fluorescence generated by said fluorophore at various locations in said multi-cellular organism by whole-body external fluorescent optical imaging;

b) determining the expression of said promoter, via observing the presence, absence or intensity of the fluorescence generated by said fluorophore at various locations

by whole-body external fluorescent optical imaging, in a control multi-cellular organism which expresses said fluorophore under the direction of said promoter of said gene; and

c) comparing the expression of said promoter determined in steps a) and b), wherein the expression determined in step a) is different from that in step b) when said test substance modulates said gene expression.

38. The method of claim 37, wherein the promoter is an endogenous promoter of the multi-cellular organism.

39. A method to screen for a multi-cellular organism that expresses a gene at an altered level, which method comprises:

a) administering a mutation-inducing agent or treatment to a non-human multi-cellular organism which expresses a fluorophore under the direction of a promoter of a gene, and determining the expression of said promoter via observing the presence, absence or intensity of the fluorescence generated by said fluorophore at various locations in said multi-cellular organism by whole-body external fluorescent optical imaging;

b) determining the expression of said promoter, via observing the presence, absence or intensity of the fluorescence generated by said fluorophore at various locations by whole-body external fluorescent optical imaging, in an untreated control multi-cellular organism which expresses said fluorophore under the direction of said promoter of said gene; and

c) comparing the expression of said promoter determined in steps a) and b), wherein the expression determined in step a) is different from that in step b) when said multi-cellular organism expresses said gene at said altered level.

40. The method of claim 39, wherein the mutation-inducing agent or treatment causes a mutation in germ-line cells of the multi-cellular organism so that the mutation is stably-transferable to offspring of the multi-cellular organism.